Nitration of pyridine by dinitrogen pentoxide, a study of the reaction mechanism†

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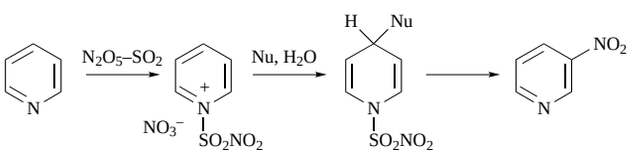
The nitration of pyridine and substituted pyridines by dinitrogen pentoxide (DNP) has been studied. The reaction of DNP with pyridine in either liquid SO_2 or an organic solvent produces *N*-nitropyridinium nitrate (4). On reaction of this with aqueous solutions of SO_2 or $NaHSO_3$ three transient species are formed: *N*-nitro-1,4-dihydropyridine-4-sulfonic acid (5), *N*-nitro-1,2-dihydropyridine-2-sulfonic acid (6) and 1,2,3,6-tetrahydro-3-nitropyridine-2,6-disulfonic acid (7). Compounds 6 and 7 may be sulfite esters instead of sulfonic acids. Compound 5 reacts by a first order reaction [$\Delta H^{\ddagger} = 32(1)$ kcal mol^{-1}, $\Delta S^{\ddagger} = 31(4)$ cal K^{-1} mol^{-1}] and 3-nitropyridine is formed. Compound 6 is rapidly transformed to 7 which reacts by a first order pH dependent reaction {$k_{obs} = 1.9(4) \times 10^{-4}$ s^{-1} + $3.5(2) \times 10^{-2}$[H$^+$] M^{-1} s^{-1}} to give 3-nitropyridine. From the available evidence the reactions were either intramolecular or took place in a solvent cage. Two mechanisms are found to be in accordance with the reported evidence: the nitro group either migrated as a nitronium ion in a solvent cage or by a sigmatropic shift. The results from the nitration of a series of dimethylpyridines support the sigmatropic shift migration mechanism.

Introduction

We have reported the successful nitration of pyridine and pyridine derivatives by dinitrogen pentoxide (N_2O_5, DNP) in the presence of sulfur dioxide.[1,2] On the basis of the data available at the time, we proposed that the nitration took place by the formation of a pyridine–SO_2–N_2O_5 complex (**1**). When this



1 **2** **3**

Scheme 1

complex was added to water, a 1,4-dihydropyridine complex was formed, formulated as **2**. We proposed two mechanisms for the reaction of **2** to give 3-nitropyridine: one by a concerted reaction *via* a six-membered transition state, another by the formation of a nitronium ion which reacted in a solvent cage to give 3-nitropyridine.[3]

By a further development of the reaction conditions, we have found it possible to first react the pyridine compound with DNP in an organic solvent without any SO_2 present and then have the product react further with an aqueous solution of a nucleophile. The nucleophiles could be SO_3^{2-}, HSO_3^- or $SO_2 \cdot xH_2O$.[4] This new procedure has several practical advantages but it also gives important information on the mechanism of this reaction. Introductory experiments showed that the predominant intermediate from the reaction in water was determined by the nucleophile used. Nevertheless, the yields of nitrated pyridine compounds were similar regardless of the applied nucleophile, for instance 63% of 3-nitropyridine (**3**) from the reaction in liquid SO_2[1] and 68% from the reaction in nitromethane followed by reaction in water–$NaHSO_3$.[4] We have therefore made further investigations into the reaction mechanism(s) for these nitration reactions.

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Results

The reaction in organic solvents

On reaction of pyridine with DNP in nitromethane or THF we obtained a compound with ^{1}H NMR data close to those reported from the same reaction in liquid SO_2 (Table 4 in Experimental section).[3] The ^{1}H NMR spectrum from that reaction was compared with the one reported by Olah *et al.* for *N*-nitropyridinium tetrafluoroborate.[5] These signals were at significantly higher field ($\delta = 8.3$, 7.5 and 7.8 for $H^{2,6}$, $H^{3,5}$ and H^4 respectively) than those observed from our reaction. We therefore concluded that the product from pyridine and DNP in liquid SO_2 was not *N*-nitropyridinium nitrate but a pyridinium–SO_2–DNP complex (**1**). In the present reaction between pyridine and DNP in $C^2H_3NO_2$ or [$2H_8$]THF without SO_2 there is no possibility for the formation of **1** and the most likely product from the reaction would be *N*-nitropyridinium nitrate (**4**). Our ^{1}H NMR data (Table 4) are indeed very close to those in more recent reports for *N*-nitropyridinium tetrafluoroborate.[6] We therefore conclude that the product from the reaction of pyridine with DNP in both liquid SO_2 and in organic solvents is *N*-nitropyridinium nitrate (**4**).

Reactions in water

***(a)* With SO_2.** When the product from the reaction of pyridine with DNP in an organic solvent was mixed with ^2H_2O saturated with SO_2 we observed the same ^{1}H NMR signals as those observed when the liquid SO_2 solution of the product from pyridine and DNP was mixed with water.[3] The product from that reaction was formulated as **2**, a 1,4-dihydropyridine derivative. From the reaction in nitromethane without SO_2 we now know that the first product in the reaction is not **1** but **4**. Furthermore, we have performed an experiment which gave information on the nature of the nucleophile Nu in structure **2**: when an acidic (pH *ca.* 1) aqueous solution of the 1,4-dihydropyridine compound was neutralized (pH *ca.* 7), **5** was transformed to the salt of pyridine-4-sulfonic acid. Therefore, the most likely structure for the intermediate formed in SO_2–water is *N*-nitro-1,4-dihydropyridine-4-sulfonic acid or its anion (**5**).

We have earlier attempted to determine the intra- or intermolecular nature of the formation of 3-nitropyridine (**3**) from **5**

Table 1 Reaction of *N*-nitro-1,4-dihydropyridine-4-sulfonic acid (**5**) to 3-nitropyridine (**3**) in water saturated with SO_2; $[\mathbf{5}]_0 = 0.14$ M

θ/°C	$k_1/10^{-5}$ s^{-1}	r^2
10	1.07(9)	0.9919
20	7.49(1)	0.9997
24[a]	16.3(1)	0.9997
25	22.8(1)	0.9998
30	38.9(9)	0.9998
35[b]	121(4)	0.9993

[a] Half the normal $[\mathbf{5}]_0$. [b] Twice the normal $[\mathbf{5}]_0$.

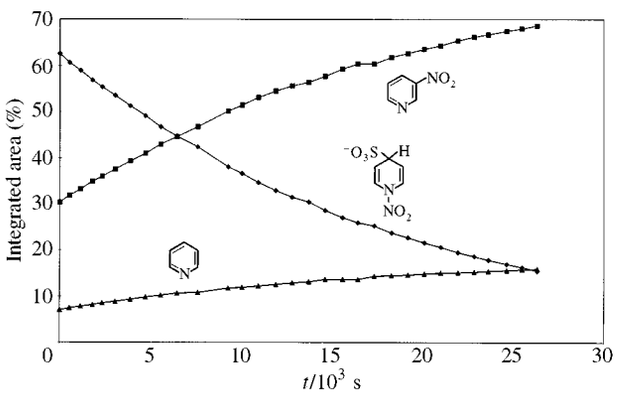
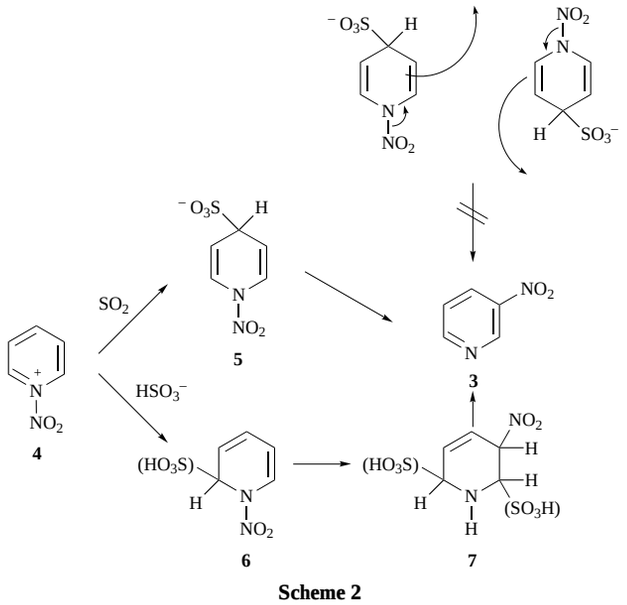


Fig. 1 Variations in the concentrations of pyridine, 3-nitropyridine (**3**) and *N*-nitro-1,4-dihydropyridine-4-sulfonic acid (**5**) with time in an experiment with SO_2 as the major nucleophile. For details see Experimental section.

by the use of cross-over experiments, by attempts to trap free NO_2 radicals by hydroquinone and by the presence of $H^{15}NO_3$ in the water phase. We did not find any evidence for an intermolecular reaction.[3] Introductory kinetic experiments also indicated the reaction of **5** to be first order. We have now carried out a more extensive kinetic investigation. The reactions were monitored by ^{1}H NMR spectroscopy with 2,4,6-trimethylpyridine as internal standard. Compound **5** reacted to give 3-nitropyridine and pyridine (Fig. 1). The ratio ([3-nitropyridine] − [3-nitropyridine]$_0$)/([pyridine] − [pyridine]$_0$) (where [3-nitropyridine]$_0$ and [pyridine]$_0$ are the concentrations at the start of the recordings) was constant during each kinetic run. The first order rate constants in Table 1 are those for the formation of 3-nitropyridine.

The experimental data gave excellent fits with the first order rate law. On the other hand, attempts to use second order rate laws gave poor fits with a pronounced curvature. Two runs at 24 and 25 °C gave similar rate constants, even if $[\mathbf{5}]_0$ for the run at 24 °C was half of that at 25 °C, again in accordance with a first order reaction. From the data in Table 1 one obtains the activation parameters: $\Delta H^{\ddagger} = 32(1)$ kcal mol^{-1}, $\Delta S^{\ddagger} = 31(4)$ cal K^{-1} mol^{-1} with $r^2 = 0.9972$ (average temp. 24 °C). Within the limits of error the rate of reaction of **5** was independent of the pH of the water phase.

***(b)* With $NaHSO_3$.** On reaction of *N*-nitropyridinium nitrate (**4**) with aqueous sodium bisulfite, a 68% yield of 3-nitropyridine was obtained, close to that from the reaction with SO_2 in water. However, the NMR spectra of the water solution showed the major intermediate in this reaction to be the 1,2,3,6-tetrahydropyridine derivative **7**: the ^{1}H NMR spectrum showed signals at 4.7, 5.0, 5.5, 6.3 and 6.4 ppm. A proton–carbon correlation spectrum showed that only the protons with signals at 6.3 and 6.4 ppm were bonded to sp^2 hybridized carbon atoms, the others to sp^3 hybridized ones (^{13}C shifts < 82 ppm). Both olefinic protons showed coupling constants to protons attached to sp^3 hybridized carbons, 4.2 and 3.0 Hz. These coupling constants are in the range of vicinal proton–proton coupling constants, placing the double bond in the 4,5-position



Scheme 2

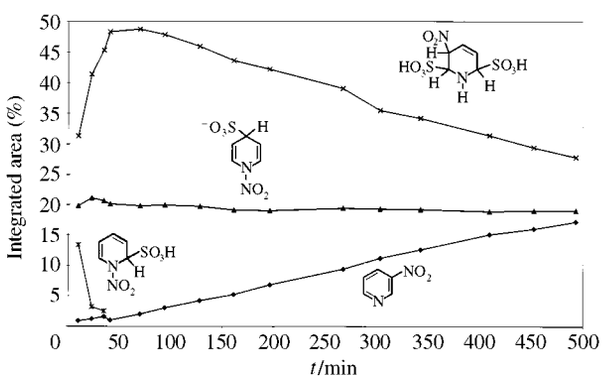


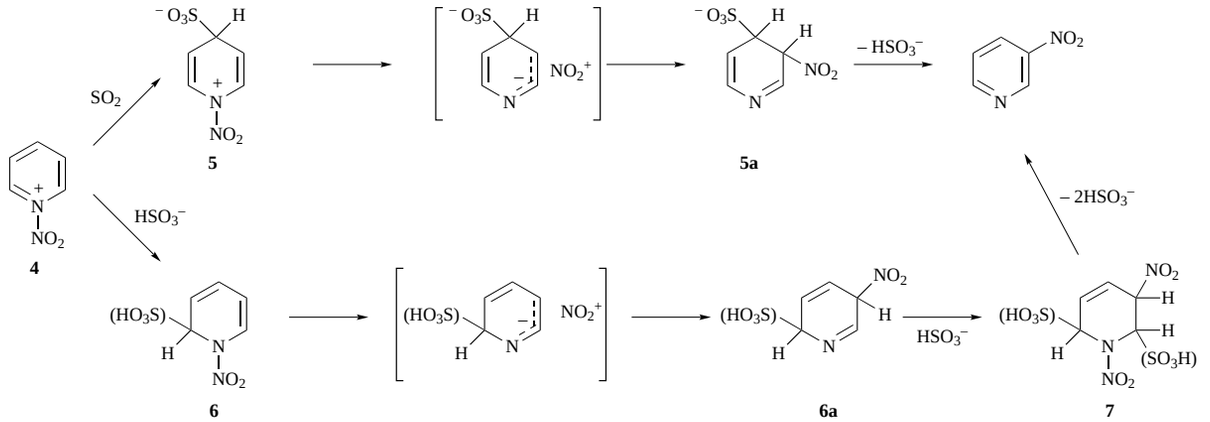
Fig. 2 Variations in the concentrations of 3-nitropyridine (**3**), *N*-nitro-1,2-dihydropyridine-2-sulfonic acid (**6**), *N*-nitro-1,4-dihydropyridine-4-sulfonic acid, (**5**) and 1,2,3,6-tetrahydro-3-nitropyridine-2,6-disulfonic acid (**7**) with time in an experiment with HSO_3^- as the major nucleophile. For details see Experimental section.

as in **7**. We will return to the identity of the substituents in the Discussion section.

By running the NMR spectra at 0 °C immediately after the addition of *N*-nitropyridinium nitrate to the $NaHSO_3$ solution another intermediate was observed. This reacted rapidly to give an increase in the concentration of **7** (Fig. 2).

By the same type of argument and the same NMR techniques as those used for the elucidation of the structure **7** this compound was given the structure **6**. Even at 0 °C compound **6** disappeared rapidly and no kinetic investigation was made of its reaction. However, compound **7** reacted at a convenient rate. Introductory experiments showed its rate of reaction to be highly dependent on the pH of the solution. The kinetic experiments were therefore run at constant pH. Under these conditions the reaction followed a first order rate law. Attempts to apply second order kinetics resulted in a poor fit with a pronounced curvature (Table 2). As the reaction was highly dependent on the pH of the solution, we expected the observed rate constant to be: $k_{obs} = k_1 + k_2[H^+]$ where k_{obs} is the observed first order rate constant, k_1 is the pH independent first order rate constant and k_2 is the second order rate constant for the proton catalysed reaction of **7**. The kinetic data are given in Table 2. From these data we obtain $k_1 = 1.9(4) \times 10^{-4}$ s^{-1} and $k_2 = 3.5(2) \times 10^{-2}$ M^{-1} s^{-1} at 25 °C.

Deuterium was not incorporated in the product from running the reaction in ^2H_2O and no solvent deuterium isotope effect was observed (Entries 4 and 5 in Table 2).



Scheme 3

Table 2 Reaction of the 1,2,3,6-tetrahydropyridine derivative **7** to 3-nitropyridine (**3**) in a ^2H_2O-solution of sodium bisulfite at 25 °C; kept at constant pH by titration with 2 M $^2HNO_3$; $[NaHSO_3]_0 = 1.10$ M

Entry	pH	$k_{obs}/10^{-4}s^{-1}$	r^2
1	1.47	14.0(3)	0.9996
2	1.75	7.14(14)	0.9985
3	2.02	5.45(8)	0.9990
4[a]	2.34	3.25(12)	0.9943
5	2.35	3.36(8)	0.9947
6	2.73	2.82(8)	0.9965

[a] H_2O used as solvent.

Discussion

From the data available at that time we had proposed the 1,4-dihydropyridine adduct **2** to be an intermediate in the formation of 3-nitropyridine.[3] We have now established that the NO_2 group is directly bonded to the ring *N*-atom (**4**). The cyclic reaction path discussed for structure **2** was therefore excluded. Furthermore, we have observed three different transient species (**5**, **6** and **7**) from the reaction of *N*-nitropyridinium nitrate with aqueous solutions of $SO_2 \cdot xH_2O$ and $NaHSO_3$.

In the reaction of **4** with $SO_2 \cdot xH_2O$ as a nucleophile the 1,4-dihydropyridine compound **5** was the only observed intermediate. Its concentration decreased with time and that of 3-nitropyridine and, to a lesser degree, that of pyridine increased (Fig. 1). On the other hand, the reaction of HSO_3^- produced the tetrahydropyridine derivative **7** as the major intermediate for the formation of 3-nitropyridine. From Fig. 2 it seems likely that this was formed from **6**, a 1,2-dihydropyridine derivative.

We will first discuss the nature of the substituents of **6** and **7**. The mode of reaction of pyridinium salts with nucleophiles is very dependent on the nucleophile, the reaction conditions and also on the *N*-substituent of the pyridinium ion.[7–9] The observation that two different major intermediates, **5** and **7** were formed on reaction with $SO_2 \cdot xH_2O$ and with $NaHSO_3$ indicate that two different nucleophiles had reacted in the two cases. The concentrations of $SO_2 \cdot xH_2O$ and HSO_3^- are dependent on the pH of the solutions [eqns. (1) and (2)]. With HSO_3^- (pH = 2.5)

$$SO_2 \cdot xH_2O = HSO_3^- + H_3O^+ \; [pK_a(1) = 1.89] \qquad (1)$$

$$HSO_3^- = SO_3^{2-} + H_3O^+ \; [pK_a(2) = 7.21]^{10,11} \qquad (2)$$

the ratio $[SO_2 \cdot xH_2O]/[HSO_3^-]$ would be *ca.* 1:4. Under these conditions, not only the tetrahydropyridine derivative **7** but also the dihydropyridine derivative **5** were observed in a 3:1 ratio. With $SO_2 \cdot xH_2O$ (pH = 1, $[SO_2 \cdot xH_2O]/[HSO_3^{-1}] \approx 8$) we only observed **5**. However, the high starting concentration of 3-nitropyridine (Fig. 1) probably reflects the starting concentration of **7** which would rapidly react to 3-nitropyridine at this low pH. At pH = 1, this would give a **7**:**5** ratio of *ca.* 0.6. Thus, the ratio **7**:**5** reflects the pH dependent ratio $[HSO_3^-]/[SO_2 \cdot xH_2O]$. From this, $SO_2 \cdot xH_2O$ gave rise to **5** and HSO_3^- to **7**. At the low pHs for these reactions, $[HSO_3^-]/[SO_3^{2-}] \approx 10^{-6}$ and $[SO_3^{2-}]$ too low for this to be important in the reaction.

The normal mode of reaction of the sulfur nucleophiles discussed here would be by the sulfur atom with formation of sulfonic acid derivatives.[12] However, in the case of the intermediate **7** a disulfite ester and not a disulfonic acid may have been formed as **7** was subject to acid catalysis and not **5** which was a sulfonic acid (see above). Furthermore, the attack of $SO_2 \cdot xH_2O$ in the 4-position of the ring was by the sulfur atom, the position expected for a soft nucleophile.[13] The expected attack of a hard nucleophile on a pyridinium ring is in the 2,6-positions.[13] For HSO_3^-, sulfur would represent the soft and oxygen the hard nucleophile and an attack of the hard oxygen atom in the 2,6-positions would give rise to sulfite esters. These points may indicate that **7** was a sulfite ester and not a sulfonic acid derivative.

From cross-over experiments, intermolecular reaction paths appeared to be ruled out and the reaction showed no kinetic deuterium isotope effect.[3] A possible intermolecular reaction which was not excluded by these experiments, exemplified by the reaction of **5**, is shown in Scheme 2: two molecules of **5** react and give 3-nitropyridine. However, this mode of reaction is eliminated by the kinetic data reported in the present study as these were not compatible with a bimolecular type of reaction. The experiments instead showed that the reactions of both the observed transient species **5** and **7** followed a first-order or pseudo first-order reaction rate law.

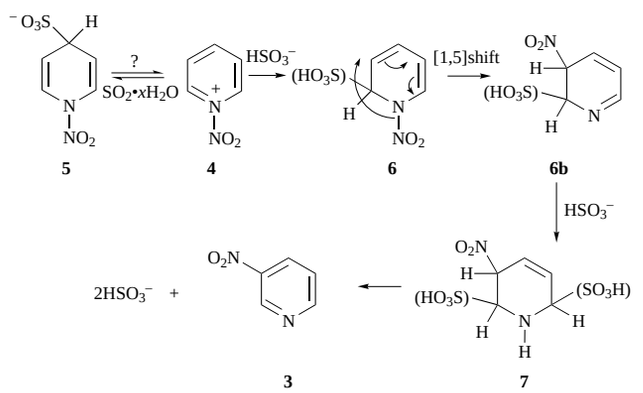
This, and the results from the various cross-over experiments are compatible with reaction paths in which NO_2 migrates from the *N*- to the β-position by either an intramolecular reaction or by a reaction in a solvent cage. In Scheme 3, an ionic reaction path is depicted. Compounds **5** and **6** have enamine structures. The nitro group leaves the pyridine *N*-atom and migrates to the nucleophilic 3-position in a solvent cage to give intermediates **5a** and **6a** (not observed). From these, 3-nitropyridine (**3**) is formed by loss of $HSO_3^-/SO_2 \cdot xH_2O$. This would presumably be an extramolecular migration as defined by Schofield for *ipso* nitration reactions.[14]

For the 1,2-dihydropyridine derivative **6**, a different reaction path would be by a [1,5] sigmatropic shift of the nitro group, from the *N*-atom to the β-position (Scheme 4). The migration from the ring nitrogen atom makes it impossible to determine the stereochemistry of the migration. From $^3J_{H(2),H(3)}$ (4.2 Hz), the substituents at C^2 and C^3 had a *cis*-configuration and one dominating stereoisomer was formed as determined by the spectra of **7**. Due to overlapping signals the formation of minor amounts of other stereoisomers was not excluded.

The reactions shown in Scheme 4 from *N*-nitropyridinium nitrate involve a [1,5] sigmatropic shift in a 1,2-dihydropyridine ring, analogous to the cyclohexa-1,3-diene system. For this,

Table 3 Nitration of dimethylpyridines with N_2O_5 in liq. SO_2 followed by quenching with water[1]

Position of CH_3 groups	Yield	Position of NO_2 group
2,3	46	5
2,4	66	5
2,5	<3	3/4 (1 : 4)
2,6	1	3
3,4	58	5
3,5	0	

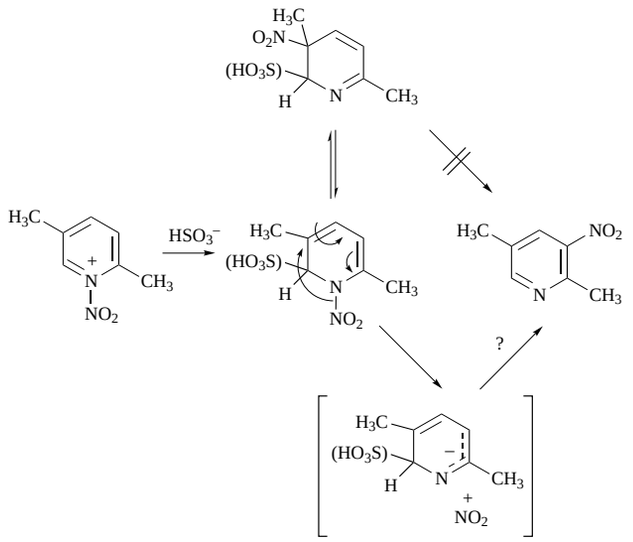


Scheme 4

several [1,5] shifts have been reported with carbon as the migrating group.[15] One [1,5] shift of a nitro group has been reported, the reaction of *N*-nitropyrazole.[16] The reaction of this compound took place at 120–150 °C. The reaction of **6** was rapid even at 0 °C. However, the reaction of *N*-nitropyrazole proceeded from an aromatic to a non-aromatic compound, but both **6** and **6b** are non-aromatic substances. The bond breaking/bond formation in sigmatropic shifts may have varying degrees of synchronicity.[17] In the case of the 2,6-shift of the nitro group in 2-methyl-2-nitrocyclohexa-3,5-dienone it was proposed that the reaction took place by a radical pair formation. The high degree of regioselectivity was explained by the participation of the 1-oxygen atom in the reaction.[18] We do not have experimental indications of the synchronicity of the present reaction. However, the high regioselectivity of the nitro group shift from the ring *N*-atom to the ring β-position is consistent with a concerted reaction as shown in Scheme 4.

The structure of the product from the NO_2 migration would be different for the two modes of reaction discussed. For the ionic reaction, a 2,5-disubstituted 2,5-dihydropyridine derivative would be formed (**6a**). For the concerted reaction the product would be a 2,3-disubstituted 2,3-dihydropyridine compound (**6b**). From the results reported here it is not possible to distinguish between these two mechanisms (Schemes 3 and 4). However, we have reported the results of the DNP–SO_2 nitration of a series of dimethylpyridines.[1] For convenience we duplicate these in Table 3. As both **5** and **6** are intermediates for the reactions run in SO_2 (see above) these results are of relevance for the reaction mechanism.

From Table 3 it is evident that the positions of the methyl groups are important for the yield of the nitration. For three of the dimethylpyridines, 2,3-, 2,4- and 3,4-dimethylpyridine good yields were obtained but for 2,6-, 2,5- and 3,5-dimethylpyridine no or very low yields of dimethylnitropyridines were obtained. From this, we deduced that neighbouring α- and β-positions needed to be free for the nitration to take place. For 2,6- and 3,5-dimethylpyridine, these results would be explained by both the proposed mechanisms (Schemes 3 and 4). However, for 2,5-dimethylpyridine, the ionic mechanism may be less satisfactory. For this mechanism the only explanation for the lack of nitration reaction appears to be the steric hindrance for the nitronium ion by the methyl group in the α-position. On the other hand, for the reaction by the concerted [1,5] nitro group shift, the β-methyl group would block the formation of 3-nitropyridine (Scheme 5).



Scheme 5

These points concern the reaction of the 1,2-dihydropyridine derivative **6**. For the 1,4-dihydropyridine intermediate **5**, two main paths of reaction would be possible: one directly to give 3-nitropyridine as indicated in Schemes 2 and 3, the other a reaction of **5** to give **6**, presumably by an equilibrium reaction of **5** with the *N*-nitropyridinium ion **4** as shown in Scheme 4. From the kinetic results reported here we know that the reaction of **6** was faster than that of **5** at the pHs applied for the nitration reaction. It would therefore not be possible to observe the transformation of **5** to **6** by the reaction of **5** with excess sodium bisulfite.

Another attempt to establish the transformation of **5** to **6** was made by a saturation transfer ^{1}H NMR experiment. By irradiation of signals from the protons in **5**, a decrease in the intensities of the signals from the corresponding protons in **6** might be observed if **5** reacts to give **6**. However, the variations in the intensities would depend on both the rate of reaction and on the rate of relaxation of the exited NMR states and would not be predictable from the available data. On irradiation of the signals from the protons on $C^{2,6}$ of **5**, a 2% decrease of the signals from the proton on C^6 and a 1.6% decrease of the signal from the proton on C^2 of **6** was observed, indeed indicating a reaction of **5** to give **6**. However, two points make this interpretation less certain. One is the low degree of saturation transfer, the other is that a decrease in the intensity (1.7%) of the signal from the proton at C^5 of **6** was also observed. This last effect cannot be explained as a simple saturation transfer effect. It may be a secondary effect originating from the disturbance of the populations of the energy levels of the proton on C^2.

We have thus not been able to demonstrate that **5** reacts to give **6**. The formation of 3-nitropyridine from **5** may instead occur directly by an ionic reaction as shown in Scheme 3 or by a [1,3] sigmatropic shift of the nitro group from the *N*-atom to the 3-position although the positive $\Delta S^{\ddagger}$ observed for the reaction of **5** does not support an ordered transition state. Sigmatropic [1,3] shifts of a nitro group in a six membered ring have been proposed, *e.g.* for the nitration of 3,4-dimethylbenzonitrile.[19]

Conclusion

The reaction of pyridine with N_2O_5 in liquid SO_2 or an organic solvent gave *N*-nitropyridinium nitrate. This reacted in water with $SO_2 \cdot xH_2O$ or HSO_3^- to give two transient species, **5** and **6**. It is proposed that these reacted by sigmatropic shifts of the

Table 4 ^{1}H NMR data for the product from the reaction between pyridine and DNP (*N*-nitropyridinium nitrate, **4**)

	δ^a			J^b/Hz	
Solvent	H^2	H^3	H^4	$J_{2,3}$	$J_{3,4}$
SO_2	9.77	8.47	9.07	6.35	7.33
$C^2H_3NO_2$	9.93	8.53	9.14	6.84	7.32
$[^2H_8]$THF	10.05	8.49	9.10	6.52	7.58
^2H_2O	9.99	8.45	9.06	6.62	7.16

^{a} Chemical shift, internal reference TMS. ^{b} Coupling constant.

nitro group or by ionic solvent cage reactions to give 3-nitropyridine. The reactions of dimethylpyridines under these conditions are better explained by the sigmatropic shift reaction mechanism (Schemes 4 and 5) than by the ionic one (Scheme 3).

Experimental

NMR spectra were recorded on Bruker DPX 300 or 400 MHz instruments. *J* Values are given in Hz. Proton–proton and proton–carbon spectroscopy were performed by cosy45 and hxco programs and saturation transfer by noemul program as installed on the Bruker instruments. Mass spectra were recorded on a AEI MS 902 double-focusing high resolution instrument. The purification of reagents and solvents and the preparation of DNP have been reported.[4]

The procedure for the reaction of pyridine with DNP in nitromethane has been reported.[4] For the kinetic runs, the slurry of *N*-nitropyridinium nitrate in nitromethane was poured into H_2O or ^2H_2O containing SO_2 (from saturation of the water phase with SO_2) or $NaHSO_3$ and also 2,4,6-trimethylpyridine as standard for the ^{1}H NMR investigations. The water phase and the nitromethane phase were shaken and the phases separated. The water phase was used for the kinetic investigations and was kept at constant temperature (±0.2 °C, Haake D8 Circulator) and pH (±0.1 units, PHM 84 Research pH meter, TTT 60 Titrator, ABU 80 Autoburette, Radiometer, Copenhagen). New samples were taken for each NMR run. The concentration of each substance in the reaction mixture was determined from the ^{1}H NMR spectrum as its signal-area relative to that of the signal from the aromatic protons of the internal standard 2,4,6-trimethylpyridine. The results from these investigations are given in Figs. 1 and 2 and in Tables 1 and 2.

Lack of incorporation of deuterium in 3-nitropyridine

Mass spectra of 3-nitropyridine obtained from reaction of *N*-nitropyridinium nitrate with $NaHSO_3$ in H_2O or ^2H_2O were identical and also identical to that reported.[3]

Identification of intermediates

The identification of the intermediate from the runs with SO_2 (**5**) has been reported.[3] Two new ones were observed in the runs with $NaHSO_3$. One (**6**) disappeared fast. However, it was possible to obtain NMR spectra: $\delta_H(^2H_2O$, 0 °C) 7.35 (d, H^6, $J_{5,6}$ 7.91), 6.58 (d, H^2, $J_{2,3}$ 6.11), 6.29 (dd, H^4, $J_{3,4}$ 9.25, $J_{4,5}$ 5.92), 6.06 (dd, H^3, $J_{2,3}$ 6.11, $J_{3,4}$ 9.25), 5.70 (ddd, H^5, $J_{2,5}$ 1.13, $J_{4,5}$ 5.92, $J_{5,6}$ 7.91); $\delta_C(^2H_2O$–$C^2H_3O^2H$, −15 °C) 126.4 (C^4), 124.1 (C^6), 120.9 (C^3), 110.9 (C^5), 71.5 (C^2). Proton–proton and proton–carbon correlation spectroscopy were used to assign the signals to the protons and carbons in **6**. The reaction of the other intermediate (**7**) showed NMR spectra: $\delta_H(^2H_2O)$ 6.41 (ddd, H^5, $J_{3,5}$ 1.23, $J_{4,5}$ 10.29, $J_{5,6}$ 3.01), 6.29 (ddd, H^4, $J_{3,4}$ 4.15, $J_{4,5}$ 10.29, $J_{4,6}$ 1.80), 5.53 (ddd, H^3, $J_{2,3}$ 4.19, $J_{3,4}$ 4.15, $J_{3,5}$ 1.23), 5.07 (d, H^2, $J_{2,3}$ 4.19), 4.77 (m, H^6); $\delta_C(^2H_2O)$ 130.9 (C^5), 124.7 (C^4), 81.7 (C^3), 71.2 (C^2), 70.8 (C^6). For structure **7** proton–proton and proton–carbon correlation spectroscopy were used to assign the signals to the corresponding protons and carbons.

Identification of the substituent in the 4-position of the 1,4-dihydropyridine intermediate 5

A slurry of *N*-nitropyridinium nitrate in nitromethane was poured into a solution of sodium bisulfite. The nitromethane phase was removed. An ^{1}H NMR spectrum of the water phase showed **5** to be present. The pH of the solution was raised to seven by the use of sodium carbonate (s). The ^{1}H NMR spectrum showed that the 1,4-dihydropyridine compound (**5**) had reacted to give pyridine-4-sulfonic acid. $\delta_H(^2H_2O$, pH 7) 8.64 (dd, $H^{2,6}$, *J* 4.60, *J* 1.65), 7.71 (dd, $H^{3,5}$, *J* 4.59, *J* 1.66), (^2H_2O, pH 1) 9.02 (d, $H^{2,6}$, *J* 5.77) 8.41 (d, $H^{3,5}$, *J* 6.65). Literature:[20] $\delta_H(^2H_2O)$ 9.25 (d, 2H, arom.), 8.62 (d, 2H, arom.) The differences in chemical shifts are assumed to be due to differences in pH of the investigated solutions.

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References

1 J. M. Bakke and I. Hegbom, *Acta Chem. Scand.*, 1994, **48**, 181; J. M. Bakke, I. Hegbom, E. Øvreeide and K. Aaby, *Acta Chem. Scand.*, 1994, **48**, 1001.
2 B. Arnestad, J. M. Bakke, I. Hegbom and E. Ranes, *Acta Chem. Scand.*, 1996, **50**, 556.
3 J. M. Bakke and I. Hegbom, *J. Chem. Soc., Perkin Trans. 2*, 1995, 1211.
4 J. M. Bakke and E. Ranes, *Synthesis*, 1997, 281.
5 G. A. Olah, J. A. Olah and N. A. Overchuck, *J. Org. Chem.*, 1965, **30**, 3373.
6 G. A. Olah, S. C. Narang, J. A. Olah, R. L. Pearson and C. A. Cupas, *J. Am. Chem. Soc.*, 1980, **102**, 3507; E. K. Kim, K. Y. Lee and J. K. Kochi, *J. Am. Chem. Soc.*, 1992, **114**, 1756.
7 V. Simánek, and V. Preininger, *Heterocycles*, 1977, **6**, 475.
8 J. Becher, *Synthesis*, 1980, 589.
9 E. Andersen, J. M. Bakke, E. Ranes and J. Riha, *Acta Chem. Scand.*, in the press.
10 F. A. Cotton and G. Wilkinson, *Advanced Inorganic Chemistry*, Wiley, New York, 5 edn., 1988.
11 *Lange's Handbook of Chemistry*, ed. J. A. Dean, McGraw-Hill, New York, 13th edn., 1985, pp. 5–16.
12 See for instance R. A. Y. Jones, *Physical and mechanistic organic chemistry*, Cambridge University Press, Cambridge, 2nd edn., 1984, p. 165.
13 I. Fleming, *Frontier Orbitals and Organic Chemical Reactions*, Wiley, Chichester, 1976, p. 66.
14 K. Schofield, *Aromatic Nitration*, Cambridge University Press, Cambridge, 1980, p. 183.
15 C. W. Spangler, *Chem. Rev.*, 1976, **76**, 187 and references cited therein.
16 J. W. A. M. Janssen, C. L. Harbraken and R. Louw, *J. Org. Chem.*, 1976, **41**, 1758.
17 K. N. Houk, Y. Li and J. D. Evanseck, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 682.
18 J. H. Ridd, S. Trevelick and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2*, 1993, 1073.
19 A. Fischer and C. C. Greig, *Can. J. Chem.*, 1974, **52**, 1231.
20 B. Boduszek, *Pol. J. Chem.*, 1992, **66**, 787.

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